

8/11/04

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=> d l4

L4 HAS NO ANSWERS

L4           STR

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Structure attributes must be viewed using STN Express query preparation.

=> s l4

SAMPLE SEARCH INITIATED 18:01:30 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 1426 TO ITERATE

70.1% PROCESSED      1000 ITERATIONS

2 ANSWERS

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:   ONLINE   \*\*COMPLETE\*\*

BATCH   \*\*COMPLETE\*\*

PROJECTED ITERATIONS:       26255 TO      30785

PROJECTED ANSWERS:           2 TO       158

L5           2 SEA SSS SAM L4

=> s l4 ful

FULL SEARCH INITIATED 18:01:34 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 27190 TO ITERATE

100.0% PROCESSED    27190 ITERATIONS

10 ANSWERS

SEARCH TIME: 00.00.01

L6           10 SEA SSS FUL L4

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

155.42

324.46

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

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FILE COVERS 1907 - 11 Aug 2004 VOL 141 ISS 7  
FILE LAST UPDATED: 10 Aug 2004 (20040810/ED)

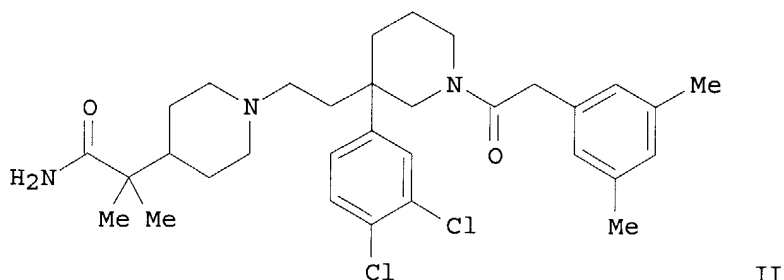
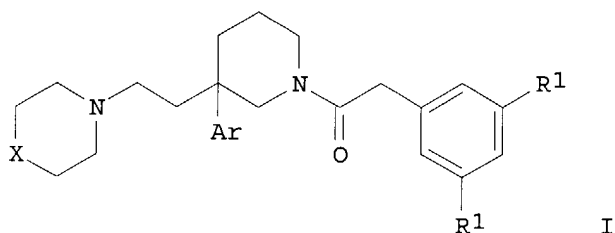
This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 16

L7 2 L6

=> d abs bib fhitstr 1-2

L7 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN  
GI



AB The invention relates to compds. I and their (in)organic acid salts, solvates and/or hydrates [wherein: X = NR<sub>2</sub> or CHR<sub>2</sub>; Ar = Ph mono- or disubstituted by halo or C1-3 alkyl; R<sub>1</sub> = Cl, Br, C1-3 alkyl, or CF<sub>3</sub>; R<sub>2</sub> = CR<sub>3</sub>R<sub>4</sub>CONR<sub>5</sub>R<sub>6</sub>; R<sub>3</sub>, R<sub>4</sub> = Me, Et, n-Pr, Bu; or CR<sub>3</sub>R<sub>4</sub> forms C3-6 cycloalkyl; R<sub>5</sub>, R<sub>6</sub> = H, C1-3 alkyl; or NR<sub>5</sub>R<sub>6</sub> = azetidin-1-yl, pyrrolidin-1-yl, piperidin-1-yl, morpholin-4-yl, thiomorpholin-4-yl, or perhydroazepin-1-yl]. The compds. exhibit a high affinity and high selectivity with respect to human NK1 receptors of substance P. The compds. are also orally active and demonstrate passage of the blood-brain barrier. The invention also relates to a method for production of I, intermediates useful in their production, pharmaceutical compns. containing them, and their use in the production of medicaments to treat all pathologies involving substance P and human NK1 receptors. Syntheses of 22 examples and a variety of intermediates are described. For instance, amidation of 3,5-dimethylphenylacetic acid with the (-)-isomer of 3-(3,4-dichlorophenyl)-3-(2-hydroxyethyl)piperidine, followed by Swern oxidation of the alc. to an aldehyde, and reductive

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amination of this with 2-(piperidin-4-yl)isobutyramide-HCl, gave title compound (-)-II.HCl.H<sub>2</sub>O. Comps. I inhibited binding of substance P to human NK1 receptors in vitro with a K<sub>i</sub> of approx. 10-11M, vs. 10-8M for NK2 receptors and 10-7 for NK3 receptors.

AN 2000:573786 CAPLUS

DN 133:177101

TI 1-[2-[1-(Phenylacetyl)-3-phenyl-3-piperidyl]ethyl]piperidine derivatives, method for the production thereof, and pharmaceutical compositions containing them as NK1 receptor antagonists

IN Ducoux, Jean Philippe; Emonds-Alt, Xavier; Gueule, Patrick; Proietto, Vincenzo

PA Sanofi-Synthelabo, Fr.

SO PCT Int. Appl., 79 pp.

CODEN: PIXXD2

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 2000047572	A1	20000817	WO 2000-FR284	20000208
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	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	FR 2789389	A1	20000811	FR 1999-1593	19990210
	FR 2789389	B3	20010309		
	FR 2789390	A1	20000811	FR 1999-4429	19990407
	FR 2789390	B3	20010309		
	CA 2360894	AA	20000817	CA 2000-2360894	20000208
	BR 2000008067	A	20011106	BR 2000-8067	20000208
	EP 1150970	A1	20011107	EP 2000-903744	20000208
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	TR 200102331	T2	20020321	TR 2001-200102331	20000208
	NZ 513053	A	20021025	NZ 2000-513053	20000208
	JP 2002536442	T2	20021029	JP 2000-598492	20000208
	EE 200100417	A	20021216	EE 2001-417	20000208
	AU 763716	B2	20030731	AU 2000-25531	20000208
	RU 2220956	C2	20040110	RU 2001-121989	20000208
	ZA 2001005829	A	20020716	ZA 2001-5829	20010716
	HR 2001000566	A1	20020831	HR 2001-566	20010726
	NO 2001003878	A	20011010	NO 2001-3878	20010808
	BG 105794	A	20020531	BG 2001-105794	20010808
	US 6642233	B1	20031104	US 2001-913106	20010809
	US 2004072840	A1	20040415	US 2003-663124	20030916
PRAI	FR 1999-1593	A	19990210		
	FR 1999-4429	A	19990407		
	WO 2000-FR284	W	20000208		
	US 2001-913106	A3	20010809		

OS MARPAT 133:177101

IT **288378-97-2P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

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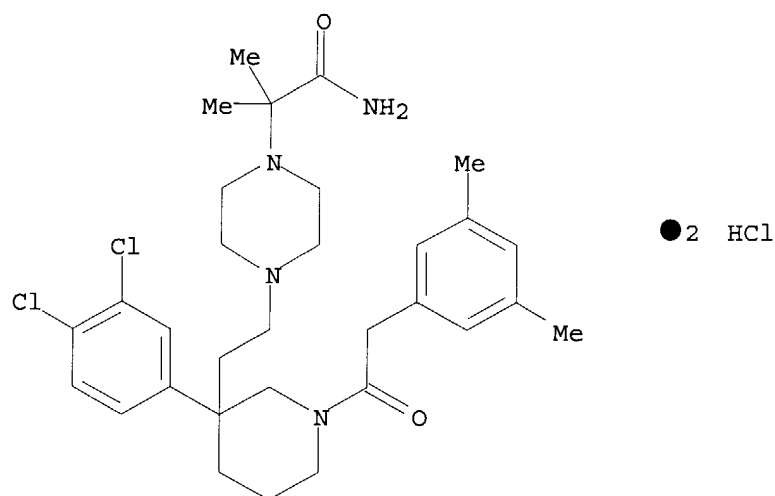
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(drug candidate; preparation of [[(phenylacetyl)phenylpiperidyl]ethyl]piperidine derivs. as NK1 receptor antagonists)

RN 288378-97-2 CAPLUS

CN 1-Piperazineacetamide, 4-[2-[3-(3,4-dichlorophenyl)-1-[(3,5-dimethylphenyl)acetyl]-3-piperidinyl]ethyl]- $\alpha,\alpha$ -dimethyl-, dihydrochloride, (-)- (9CI) (CA INDEX NAME)

Rotation (-).



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD  
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L7 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN

AB To rapidly gain information on structure-activity relation (SAR) requirements of the human neurokinin 3 (hNK-3) receptor antagonist SR 142801, an indexed combinatorial library was synthesized in solution and screened on the hNK-3 receptor. SAR considerations drawn from binding affinity of combinatorial mixts. were confirmed through the synthesis and biol. evaluation of some individual compds.

AN 1999:745214 CAPLUS

DN 132:131772

TI Investigation of SAR requirements of SR 142801 through an indexed combinatorial library in solution

AU Raveglia, Luca F.; Vitali, Mauro; Artico, Marco; Graziani, Davide; Hay, Douglas W. P.; Luttmann, Mark A.; Mena, Renzo; Pifferi, Giorgio; Giardina, Giuseppe A. M.

CS Department of Medicinal Chemistry, SmithKline Beecham S.p.A., Milan, 20021, Italy

SO European Journal of Medicinal Chemistry (1999), 34(10), 825-835  
CODEN: EJMCA5; ISSN: 0223-5234

PB Editions Scientifiques et Medicales Elsevier

DT Journal

LA English

IT **256497-35-5P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

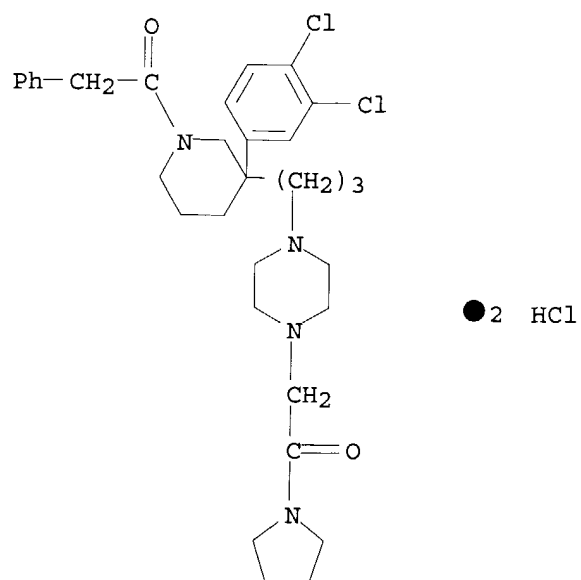
(structure-activity relation requirements of SR 142801 as neurokinin 3 receptor antagonists through indexed combinatorial library in solution)

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RN 256497-35-5 CAPLUS

CN Piperidine, 3-(3,4-dichlorophenyl)-3-[3-[4-[2-oxo-2-(1-pyrrolidinyl)ethyl]-1-piperazinyl]propyl]-1-(phenylacetyl)-, dihydrochloride (9CI) (CA INDEX NAME)



RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD  
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**European Journal of Medicinal Chemistry**  
Volume 34, Issue 10, October 1999, Pages 825-835

doi:10.1016/S0223-5234(99)00210-X [? Cite or Link Using DOI](#)  
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# Investigation of SAR requirements of SR 142801 through an indexed combinatorial library in solution

Luca F. Raveglia<sup>EF, a</sup>, Mauro Vitali<sup>c</sup>, Marco Artico<sup>a</sup>, Davide Graziani<sup>a</sup>, Douglas W. P. Hay<sup>b</sup>, Mark A. Luttmann<sup>b</sup>, Renzo Mena<sup>a</sup>, Giorgio Pifferi<sup>c</sup> and Giuseppe A. M. Giardina<sup>a</sup>

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Received 3 May 1999; accepted 25 May 1999. Available online 9 May 2000.

**Abstract**

To rapidly gain information on structure-activity relationship (SAR) requirements of the human neurokinin 3 (hNK-3) receptor antagonist SR 142801, an indexed combinatorial library was synthesised in solution and screened on the hNK-3 receptor. SAR considerations drawn from binding affinity of combinatorial mixtures were confirmed through the synthesis and biological evaluation of some individual compounds.


**Author Keywords:** tachykinins; neurokinin 3 receptor antagonists; combinatorial chemistry; indexed libraries; structure-activity relationships

**Further Reading**

[14]. (a) Calculated utilising the average molecular weight. (b) Calculated as the sum of the

areas of the seven peaks of the LC/UV chromatogram, attributed by LC/MS to the seven compounds forming each mixture.

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 Correspondence and reprints

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Volume 34, Issue 10 , October 1999, Pages 825-835

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